

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of claims:

1. (Currently amended) A method of modifying biological and/or synthetic membranes or liposomes, or combinations thereof, for the purpose of altering immunity, or for the targeting of drugs and other agents to a specific cell type or tissue when administered *in vivo* to achieve a specific therapeutic effect, said method comprising incorporating amphiphilic molecules into the said membrane or liposomes, wherein a proportion of the amphiphilic molecules have been modified by a covalent attachment of a metal chelating group to provide a chelator lipid such that at least some of the metal chelating groups are oriented toward the outside surface of said membrane or liposomes, which method also comprises the step of interacting a ~~receptor-domain~~ molecule to be engrafted which is covalently attached to a polypeptide tag with said membrane or liposomes for a time and under conditions sufficient for said polypeptide tag to attach to said membrane or liposomes *via* the outwardly facing metal chelating residues of said membrane or liposomes, such that the ~~receptor-domains are~~ engrafted molecule is capable of interacting specifically with a ligand molecule that exists on a particular cell type or tissue within the body.

2. (Currently amended) ~~A~~ The method according to Claim 1 wherein the specific interaction between the ~~receptor-domains~~ engrafted molecule and associated said membrane provides a means of altering immunity when used as vaccines, or of targeting membrane-encapsulated/incorporated drugs and other agents to specific cells or tissues when administered *in vivo* for therapeutic purposes or for modifying a physiological response or biological function.

3. (Cancelled).

4. (Currently amended) ~~A~~ The method according to Claim 3 comprising the steps of:

- (i) incorporating the chelator lipid, either alone or as a mixture of the chelator lipid and other amphiphilic molecules or

phospholipids, into the membrane to provide a membranous structure by mixing and/or co-incubation, or by production of the membranous structure from a composite mixture of lipids comprising a chelator lipid and one or more other lipids or phospholipids; and

- (ii) interacting ~~a targeting~~ said molecule to be engrafted with said membranous structure for a sufficient time and under suitable conditions to attach to said membranous structure *via* the outwardly facing metal chelating ~~residues~~ groups of said membranous structure, such that the ~~receptor domains or targetable molecules are~~ engrafted molecule is capable of interacting with a specific type of cell and/or tissue when administered *in vivo* for therapeutic purposes, or for modifying a biological response.

5. (Currently amended) A The method according to Claim 4 wherein the ~~targeting~~ engrafted molecule is a receptor domain and/or other ~~targetable~~ targeting molecule engineered to possess a metal binding polypeptide tag.

6. (Cancelled).

7. (Currently amended) A The method according to Claim 1 wherein the membranous structure is a suspension of micelles or liposomes formed from the amphiphilic molecules by sonication, or extrusion/filtration techniques.

8. (Currently amended) A The method according to Claim 3 wherein the metal chelating group is nitrilotriacetic (NTA).
9. (Cancelled).
10. (Currently amended) A The method according to Claim 1 wherein the amphiphilic molecules in the biological and/or synthetic membrane or liposomes are surfactant molecules having a hydrophilic head portion and one or more hydrophobic tails.
11. (Currently amended) A The method according to Claim 1 wherein the polypeptide tag comprises a sequence of amino acid residues that can bind to the metal chelating groups attached to the said biological and/or synthetic membrane or liposomes.
12. (Currently amended) A The method according to Claim 11 wherein the amino acid residues are histidine residues.
13. (Currently amended) A The method according to Claim 11 wherein the polypeptide tag comprises at least five amino acid residues.
14. (Currently amended) A The method according to Claim 13 wherein the polypeptide tag comprises at least six amino acid residues.
15. (Currently amended) A The method according to Claim 14 wherein the polypeptide tag comprises hexa-histidine.
16. (Withdrawn) A method of modifying biological and/or synthetic membranes by incorporation or attachment of metal chelating groups for: (i) vaccine development; (ii) for modification of biological response(s); and/or (iii) for targeting of drugs or agents to specific tissue or cell types within the body to achieve a therapeutic effect, said method comprising:-

- (i) preparing a suspension of liposomes with chelator lipid incorporated and with or without an encapsulated drug or agent;
- (ii) incubating the liposomes with a recombinant protein or target molecule bearing an appropriate metal affinity tag; and
- (iii) if necessary, removing excess protein or molecule by washing, filtering or other washing means and suspending them in a solution appropriate for administration *in vivo*.

17. (Withdrawn) A method according to Claim 16 wherein the molecules engrafted, anchored, incorporated, or encapsulated within the liposome are therapeutic molecules, pharmaceutical compounds, DNA and/or RNA.

18. (Withdrawn) A method according to Claim 17 wherein the targeting molecules engrafted or anchored onto the liposome surface is VEGF or its homologue.

19. (Withdrawn) A method according to Claim 18 wherein the liposomes are made to encapsulate/incorporate a cytotoxic drug or agent together with the engrafted VEGF or its homologue, to block the growth of new blood vessels required for the growth of tumours.

20. (Withdrawn) A method according to Claim 19 wherein the liposomes comprise an immunogenic agent and together with an agent which targets the liposome to different cell types in the body including immune cells and tumor cells to alter immunogenicity or immunological responses.

21. (Currently amended) A method of ~~anchoring~~ engrafting a recombinant molecule directly onto cells or biological membranes, said method comprising:-

- (i) preparing a suspension of chelator lipid or liposomes containing the chelator lipid;
- (ii) incubating a suspension of cells or biological ~~membranous structures~~ membranes with a suspension of the chelator lipid to allow the chelator lipid to incorporate into the structures;
- (iii) washing away excess or unincorporated lipid;
- (iv) incubating the cells or ~~membranous structures~~ biological membranes with a solution of said recombinant ~~protein or target molecule possessing wherein said molecule possesses~~ an appropriate metal affinity tag; and
- (v) washing away excess or unbound ~~soluble protein~~ recombinant molecule, and suspending the cells or ~~structures~~ biological membranes in a solution suitable for administration *in vivo*.

22. (Withdrawn) A method according to Claim 21 wherein the recombinant molecule is a co-stimulatory molecule.

23. (Currently amended) A ~~The~~ method according to Claim 21 wherein the biological membrane is from a tumor cell.

24. (Currently amended) A ~~The~~ method according to Claim 21 for use in enhancing or modifying immunity to tumors, for modifying any biological response, or for the treatment of any disease condition.

25. (Currently amended) A ~~The~~ method according to Claim 21 wherein the recombinant molecule is a receptor or ligand.

26. (Currently amended) A The method according to Claim 21 wherein the recombinant molecule is a ligand for a receptor on specific cell types within the body or on cells such as tumor cells that arise as a consequence of disease.

27. (Currently amended) A method for altering the immunogenicity of a ~~target~~ cell or membranous component thereof, said method comprising ~~anchoring~~ engrafting a molecule to the membrane of said ~~target~~ cell by:-

- (i) preparing a suspension of chelator lipid or liposomes containing the chelator lipid;
- (ii) incubating a suspension of said cells or membranous ~~structures~~ component thereof with a suspension of the chelator lipid;
- (iii) washing away excess or unincorporated lipid;
- (iv) incubating the said cells or membranous ~~structures~~ component thereof with a solution of said molecule to be ~~anchored~~ engrafted; and
- (v) washing away excess or unbound ~~soluble~~ molecule, and suspending the ~~structures~~ cells or membranous component thereof in a solution suitable for administration *in vivo*.

28. (Currently amended) A The method according to Claim 27 wherein the ~~target~~ cell or membranous component thereof is a tumor cell.

29. (Currently amended) A The method according to Claim 27 wherein the molecule is a ligand, receptor, recombinant protein, polysaccharide, glycoprotein or antigen.

30. (Currently amended) A method of targeting ~~cells or biological and/or synthetic membranes or liposomes~~ a membranous structure to a particular cell type or tissue within the body, wherein said membranous structure comprises cells or biological and/or synthetic membranes or liposomes, said method comprising ~~anchoring or engrafting to said membranous structure~~ a molecule having a binding partner on the particular cell type or tissue to be targeted by:-

- (i) preparing a suspension of chelator lipid or liposomes containing the chelator lipid;
- (ii) incubating a suspension of ~~cells or the biological or synthetic~~ membranous structures with a suspension of the chelator lipid;
- (iii) if necessary, washing away excess or unincorporated lipid;
- (iv) incubating the ~~liposomes or~~ membranous structures with a solution of ~~molecules~~ said molecule to be ~~anchored~~ engrafted;
- and
- (v) washing away excess or unbound ~~soluble~~ molecule, and suspending the structures in a solution suitable for administration *in vivo*.

31. (Currently amended) A method of treatment, said method comprising administering to a subject an effective amount of a liposome preparation or membranous material comprising an active material and optionally an ~~anchored or~~ engrafted molecule having a binding partner ~~or on~~ target tissue.

32. (Currently amended) A The method according to Claim 31 wherein the active material is a recombinant polypeptide, co-stimulatory molecule, therapeutic drug or nucleic acid molecule, either engrafted onto the surface or encapsulated/incorporated within the liposome or membranous material.

33. (Currently amended) A The method according to Claim 31 wherein the ~~anchored~~ ~~or~~ engrafted molecule is a receptor, ligand, glycoprotein, polysaccharide or recombinant polypeptide.

34. (Currently amended) A The method according to Claim 33 wherein the anchored molecule is VEGF.

35. (Currently amended) A The method according to Claim ~~27~~ when used 31 wherein said treatment is to enhance immunity to a specific tumor or disease.

36. (Withdrawn) A method according to Claim 32 wherein the co-stimulatory molecule is CD40 or B7.1.

37. (Withdrawn) A vaccine composition comprising cells or membranous material having engrafted thereto molecules capable of modifying an immunological response to a subject to which the vaccine is administered, said vaccine further comprising one or more pharmaceutical carriers and/or diluents.

38. (Withdrawn) A vaccine according to Claim 37 wherein the molecules engrafted to the cells or membranous material are co-stimulatory molecules.

39. (Withdrawn) A vaccine according to Claim 37 prepared by the steps of:

- (i) incubating the liposomes, cells or membranous material with a chelator lipid such as NTA-DTDA, or a mixture of



amphiphilic molecules containing a chelator lipid, to allow the lipid to incorporate in the cells or membranes;

- (ii) washing off any unincorporated lipid by centrifugation or filtration and resuspension of the liposomes, cells or membranous structures in the appropriate solution or buffer;
- (iii) incubating the liposomes, cells or membranous structures with incorporated chelator lipid with said molecules to be engrafted; and
- (iv) washing off unincorporated molecular material.